

Functional and behavioral correlates of the mirror *Paired Associative Stimulation* protocol

Guidali Giacomo^{1,2} & Bolognini Nadia^{1,3}

¹ Department of Psychology, University of Milano-Bicocca & Milan Center for Neuroscience – NeuroMI, Milan, Italy.

² PhD program in Neuroscience, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy.

³ Laboratory of Neuropsychology, IRCCS Istituto Auxologico Italiano, Milan, Italy.

Background. Hebbian associative plasticity has been implied in the formation of the association between sensory and motor representations of actions in the Mirror Neuron System (MNS). Recently, our research group developed a novel *Paired Associative Stimulation* (PAS) protocol targeting the MNS: the mirror PAS (m-PAS) [1]. The m-PAS repeatedly pairs TMS pulse over the right M1 with visual stimuli depicting movements made with the right hand (ipsilateral to TMS cortical site). The m-PAS successfully induced new ipsilateral motor resonance responses, indexed by an atypical [2] facilitation of cortico-spinal excitability by the view of ipsilateral (right) hand movements – i.e., the ones conditioned during the protocol. **Aims.** To deepen the functional correlates of such a protocol, we run two experiments exploring its visual and cortical specificity, hence modulating the visual stimulus (*Experiment 1*) and the site of TMS administration during the protocol (*Experiment 2*). In *Experiment 2* we also explored possible effects of the m-PAS on behavior, exploiting an imitative compatibility task assessing *automatic imitation* [3]. **Methods.** Thirty-five healthy participants were tested in the two experiments (20 in *Experiment 1* and 15 in *Experiment 2*). In *Experiment 1*, besides the standard m-PAS, a control version was tested in which the visual stimulus depicted a moving pair of scissors (non-biological movement). In *Experiment 2*, in the control protocol, TMS was delivered over the left M1. In both experiments, before and after each PAS session, motor resonance was assessed by recording Motor Evoked Potentials (MEPs) induced by single-pulse TMS applied to the right M1, during the observation of both contralateral (left) and ipsilateral (right) index-finger movements or static hands. In *Experiment 1*, motor resonance was also recorded during the observation of a static/moving pair of scissors. In *Experiment 2*, before and after each m-PAS, participants also performed an imitative compatibility task taken from previous literature. **Results.** Results showed the efficacy of the standard m-PAS in inducing the emergence of motor resonance for the conditioned, ipsilateral (to TMS), index-finger movement. Crucially, this effect is not present when the visual stimulus is a non-biological one (*Experiment 1*) and TMS is delivered over the contralateral (to the observed movement) hemisphere (*Experiment 2*). Importantly, m-PAS also affects behavior, modulating *automatic imitation* (indexed as the difference between reaction times in incongruent and congruent trials of the imitative compatibility task) when a right hand is observed. **Conclusion.** Our results corroborate the evidence that the visual-motor matching properties of the MNS can be shaped by the m-PAS protocol, suggesting possible modulations also at a behavioral level.